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CAUSES AND COMMON CLINICAL PRESENTATION OF CHILDREN WITH SPLENOMEGALY IN KHARTOUM STATE

A thesis submitted in partial fulfillment for the requirements of the degree of

Clinical MD in Pediatrics and Child Health

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Dedication

To: My Dear Parents,

Brothers and Sisters &

All children in my country

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ABSTRACT

This is a prospective, descriptive hospital-based study, conducted in a period of six months (Feb-July 2005).

The study aimed to determine the common clinical presentation and the causes of splenomegaly in those children and to study the investigations that were done in these hospitals.

It included 217 children with splenomegaly, ages ranged from 0-16 years and who were attending the Pediatrics Hospitals in Khartoum State. Hematological investigations were done for every child and specific investigations were done according to the clinical findings such as Hb electrophoresis, Mantoux test, abdominal Ultra sound and bone marrow aspiration or biopsy.

The study showed an obvious male predominance, male to female ratio was 1.7:1. The majority of patients (41.5%) belong to Arab tribes and most of them (79.3%) were of low social class. The main presenting symptoms were fever (96.3%) followed by abdominal pain (55.8%), abdominal distension (47.9%), general ill health (47.9%), bone pain (32.7%) and weight loss (31.8%). The main clinical signs were pallor (83.9%), Hepatomegaly (91.2%), abdominal distension (75.6%), dyspnoea (31.8%), jaundice (23.5%) and lymphadenopathy (20.7%). Other signs such as ascites, visible dilated abdominal veins and clubbing of fingers were less detected.

Haemolytic anaemias were the commonest cause of splenomegaly in the study group (22.1%) followed by Malaria (10.6%), cardiac diseases (10.1%), Leukaemias (06.9%), Schistosomiasis (05.2%), Visceral leishmaniasis (06.0%), Tuberculosis (04.1%). Other infectious diseases rather than these, Lymphomas, Tropical splenomegaly syndrome, Iron deficiency anaemia, Liver diseases and other rare diseases such as Myelofibrosis were less reported. No definite cause was found in (12.4%).

The majority of the patients (99.1%) received medical treatment according to the cause of splenomegaly and only (0.9%) had surgical treatment. The short term out comes of patients in the study group showed that stable patients were (37.8%), recovered completely (31.3%), improved (18.0%), lost for follow up (11.2%) while (01.8%) had died.

ملخص الأطروحة

أجريت هذه الدراسة المستقبلية ، الوصفية والمعتمدة علي المستشفيات خلال ستة اشهر في الفترة من فبراير-يوليو لعام 2005 بمختلف مستشفيات وعنابر الأطفال بولاية الخرطوم .

هدفت هذه الدراسة إلى تحديد أسباب تضخم الطوحال واكثر الأعراض والعلامات السريرية المصاحبة له. كما هدفت أيضا لدراسة الاختبارات المعملية التي تجري لهؤلاء المرضي بمستشفياتهم. تم إجراء الفحوصات العامة مثل تعداد كريات الدم الكامل ،فحص البول والبراز لكل الأطفال قيد الدراسة وبعض الفحوصات الخاصه حسب الحـوجه السريريه مثـل فحـص المنجليات فـي الـدم، الرحلان الكهربائي لخضاب الدم ،الاختبار الجلدي للسل، التصوير فوق الصوتي للبطن وبذل نخاع العظم .

قد شملت الدراسة 217 طفل تتراوح أعمارهم ما بين صفر- 16 سنه ويعانون من تضخم الطوحال.

أظهرت الدراسة إن تضخم الطحال أكثر في الأطفال الذكور حيث أن نسبة الذكور للإناث 1:107 واكثر الأعمار تعرضاً هي الفئة العمرية (0-< 5سنوات). الأطفال الأكثر تعرضاً لحدوث تضخم الطحال ينحدرون من قبائل عربية(41.5%) وغالبية هؤلاء الأطفال (79.3%) ينتمون إلي أسر فقيرة. الحمى سجلت كأكثر الأعراض حدوثاً (96.3%). يليها آلم البطن (55.8%)، انتفاخ البطن (47.9%)، اعتلال الصحة العام (47.9%)،نقصان الوزن (31.8%) أكثر العلامات السريرية شيوعاً هي شحوب اللون (83.9%)، تضخم الكبد (91.2%)، انتفاخ البطن (75.6%)، زلـة التنفس (31.8%)، اليـرقان (23.5%) ، تضخـم الغـدد اللمـفاوية (20.7%). العلامات السريريه الأخرى مثل توسع الأوردة السطحية بالبطن ووجود سائل حبنى بالبطن وجدت بنسبة اقل.

فقر الدم الانحلالي (22.1%) وجد من اكثر الأسباب شيوعا تليه البرداء (10.6%)، أمراض القلب (10.1%)، الأمراض السرطانية مثل ابيضاض الدم الحاد والمزمن (6.9%). الأمراض المعدية مثل خمي التيفويد وداء البروسيلات والتهاب السحايا الحاد، داء اللشمانيا الحشوى، داء المنشقات، الدرن، الورم الليمفي، تضخم الطوحال المدارى، أنيميا عوز الحديد ،أمراض الكبد , تليف نخاع العظم، داء قوشر، الذأب الحمامي المنتشر، خمول الغدة الدرقية وفرفرية قلة الصفيحات المزمنة قد سجلت بنسبة اقل. أما الأطفال الذين لم يتم معرفة أسباب تضخم الطوحال لديهم فقد بلغت نسبتهم (12.4%) .

معظم الأطفال (99.1%) تلقوا علاجاً طبياً بينما (0.9%) تلقوا علاجاً جراحياً بإزالة الطوحال. الناتج المرضي في هذه الدراسة تراوح ما بين الشفاء التام (31.3%)، استقرار الحالة (37.8%) تحسن الحالة (18.0%)، فقد المتابعة (11.1%) والوفاة بلغت نسبتها (1.8%) . خلصت هذه الدراسة إلى أن مثل هؤلاء الأطفال يحتاجون إلى الدعم المادي بتوفير الاجهزه الخاصة لإجراء جميع الفحوصات التـي تساعد في تشخيص الحالات المبهمة وتوفير اللقاحات الخاصة بمثل هذه الحالات .

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LIST OF ABBREVIATIONS

APP	American Acadamy of paediatrics
AIDS	Aquired immunodeficiency syndrome
ALT	Alanine amino Transferase
AST	Aspartate Amino Transferase
CBC	Complete Blood Count
CMV	Cytomegalo Virus
CT	Computed Tomography
EBV	Ebstien Barr Virus
ESR	Erythrocyte sedimentation rate
G6PD	Glucose-6- phosphate dehydrogenase deficiency
Hb	Haemoglobin level
HD	Hodgkin Disease
HIV	Human Immuno deficiency virus
HS	Herediatary Spherocytosis
IGM	Immuno Globulin M
ITP	Idiopathic Thrombocytopenic Purpura
LFT	Liver Functions Test
MPS	Mononuclear- Phagocyte-system
MRI	Magnetic Resonance Imagin
NPC	Nimann- Pick Type C
RBCs	Red Blood Cells
SLE	Systemic Lupus Erythematosus
TWBC	Total White Blood Cell

1. INTRODUCTION AND LITERATURE REVIEW

1.1 ANATOMY OF THE SPLEEN:

The spleen is the largest lymph node in the body. Its anatomy provides for a uniquely close contact between its immunologic tissues and blood. Generally it's ovoid in shape. It is situated in the left hypochondrium and lies under the cover of the ninth, tenth and eleventh ribs. Its long axis corresponds to that of the tenth rib and in the adult it does not normally project forward in front of the midaxiallary line. In infants the lower pole of the spleen may just be felt. It has a notched anterior border and it is surrounded by peritoneum. The arterial blood supply is from the splenic artery[1,2].

The splenic tissue consists of red and white pulp lying within a capsule. The white pulp, rich in T- and B- cell lymphocytes, is supplied by central arterioles. These vessels tend to branch at right angles, resulting in the preferable skimming of plasma into the white pulp for antigen processing. The main terminal splenic arteries, which contain the remaining hemoconcentrated blood, continue directly forward into the contiguous red pulp .The red pulp makes up the majority of splenic tissue, consisting of splenic cords that interdigitate between splenic venous sinusoids. At least 90% of the hemoconcentrated blood reaching the red pulp enters these splenic cords, which contain a fibrous network of mononuclear - phagocyte

tissue. The circulation in the cords is designated as open because no well-defined endothelial lining exists. The cords lie between and share a basement membrane with the adjacent splenic venous sinuses[3,4].

To exit the cords, blood must pass through 1- to 5- μm slits in this fenestrated basement membrane to reach the sinuses. The circulation through the cords is slow and congested because the blood reaching the red pulp is hemoconcentrated and the erythrocytes require additional time to pass through the small and limited number of slits that must be traversed to reach the sinuses. This delay provides prolonged exposure of blood cells, bacteria and particulate matter to the dense mononuclear-phagocyte elements within the red pulp. This anatomic arrangement and the fact that the spleen (with an average of only 180-g in adults) receives approximately 6% of the cardiac out put provide a tremendous filtration capability. After blood reaches the sinuses, it passes into the splenic venous system. Blood from the sinuses enters trabecular veins and eventually the hepatic portal vein; no valves exist in this system, which remain at the same pressure as the hepatic portal vein[5,6].

1.2. PATHOPHYSIOLOGY AND FUNCTIONS:

Although none of the spleen's individual cells are unique, the spleen's distinctive anatomic arrangement provides it with characteristic functional capabilities[5,6,7].

The functions of the spleen can be categorized into 3 main functions as follow:

1.2.1. Resistance to Infection:

The spleen plays a major role in the processing of small doses of particulate and polysaccharide antigens that reach it through its vascular supply. Splenic macrophages efficiently ingest these antigens and deliver them to the immunocompetent cells of the spleen for antibody production. There is some suggestion that the spleen is the principal producer of auto-antibodies aimed at circulating blood cells which has been confirmed only for antiplatelet antibodies[7,8].

1.2.2. Filtering of formed elements of blood:

One of the primary functions of the spleen is filtration of defective cells. Erythrocytes make slow passage through the hypoxic and acidotic environment of the cords and then squeeze through narrow slits into the sinusoids. Although healthy erythrocytes readily accomplish this, many aged and abnormal red blood cells remain behind to be ingested by the macrophages lining the cords. Abnormal cells such as spherocytes, sickle cells, antibody coated erythrocytes or platelets (especially those with light

coatings 1gG) are mainly cleared by the spleen. The splenic cords also are uniquely capable of removing erythrocytic inclusions such as nuclear remnants (i.e. Howell-Jolly Bodies) or precipitated globin (i.e. Heinz Bodies), without destroying the cell[8,9].

1.2.3. Other functions of the spleen:

Other splenic functions include remolding of reticulocytes, hematopoiesis during early fetal development and functioning as a reservoir for platelets and plasma proteins such as Factor VIII. Its function as reservoir for erythrocytes is insignificant, except in pathologic states such as hypersplenism. Immunoglobulins, properdin and tufts in are produced in the spleen. The spleen has a minor role in antibody responses to intramuscularly or subcutaneously injected antigens but it is required for early antibody production after exposure to intravenous antigens. Thus young (nonimmune) or hyposplenic individuals are at increased risk for sepsis caused by pneumococci and other encapsulated bacteria[9,10].

Responses of the spleen to antigens are similar to those of lymph nodes. The major difference being that the spleen is the major site of immune responses to blood-borne antigens, while lymph nodes are involved in responses to antigens in the lymphatic circulation[8,9,10].

1.3. SPLENOMEGALY:

Splenomegaly occurs when the size of the spleen is increased by cells or tissue components or by vascular engorgement. This augments its filtering function and even normal blood cells experience a delayed transit and temporary sequestration. The sequestration of granulocytes and platelets causes neutropenia and thrombocytopenia, but these cells appear to tolerate their prolonged stay in the spleen. The trapped red cells on the other hand are usually destroyed causing haemolytic anemia. Enlargement of the spleen may be associated with hypersplenism, which occurs with an increase of filtration and macrophage surveillance in the red pulp and antibody synthesis in the white pulp[11].

In children splenomegaly usually results from hyperplasia of the mononuclear-phagocyte system (MPS) which can be categorized as excessive antigenic stimulation disorders, excessive destruction of abnormal blood cells and disorders of immunoregulation. The spleen is rarely the primary site of a disease. It is usually being affected by a systemic process involving lymphoid tissues. Splenomegaly due to a variety of causes usually increases the proportion of blood channeled through red pulp causing inappropriate hypersplenic sequestration of both normal and abnormal blood cells. The platelets are particularly likely to be sequestrated by an enlarged spleen and up to 90% of the total number of platelets in the blood may be in the spleen[12,13,14].

1.3.1. Causes of Splenomegaly:

1.3.1.1. Infections:

- Viral infections are frequently associated with splenomegaly which is usually transient and only mild to moderate in severity such as Cytomegalovirus (CMV), Toxoplasmosis, Herpes simplex and Ebstien-Barr Virus[15,16].
- Acquired Immunodeficiency Syndrome (AIDS) which is less common but is an increasingly important cause of splenic enlargement[7,17].
- Malaria and Schistosomiasis are the commonest causes of splenomegaly in endemic areas. Omer in Sudan in 1978 reported a significant increase in the frequency of splenomegaly with the presence of Schistosoma infection in the very young age group (5-9 years) in an endemic area[18,19,20].
- Other common infectious causes include bacterial, protozoal and fungal infections such as Salmonella, Brucella and Mycobateria[21,22,23].

1.3.1.2. Neoplastic disorders:

Neoplastic disorders may present with splenomegaly. One half of children with acute lymphoblastic leukemia have splenomegaly, which also

occurs in the lymphomas and acute myeloblastic leukemia. Metastatic involvement of the spleen, which is uncommon in children, is most often caused by neuroblastoma and Langerhans Cells Histocytosis[24,25].

1.3.1.3. Portal Hypertension:

This is usually due to impaired venous blood flow in the splenic or portal venous system. It can be prehepatic like thrombosis of the portal vein which is usually occurs because of inappropriate placement of an umbilical venous catheter in a sick neonate. It can be also intrahepatic like biliary atresia, metabolic infilterative disorders and alpha-1-antitrypsin deficiency or post hepatic disorders such as Budd-chiari syndrome[26,27].

1.3.1.4. Storage Diseases:

Storage diseases such as Gaucher or Niemann-Pick (NPC) disease are associated with splenomegaly because of the accumulation of abnormal lipid in the splenic macrophages. (NPC) can present with isolated splenomegaly. Also it should be considered in all infants with cholestasis, particularly those with splenomegaly. Because of the genetic nature of the disease, it is important to consider this diagnosis in all patients with splenic enlargement[28,29].

1.3.1.5. Trauma:

After trauma palpable subcapsular hematomas may develop in the spleen. It has been the most injured organ with blunt abdominal trauma[30,31].

1.3.1.6. Splenic Cysts and Tumors:

Congenital splenic cysts usually present with asymptomatic splenomegaly. In the absence of systemic illness or malignancy, splenic cysts must be considered especially the epithelial variety. Primary splenic tumors are rare and usually benign. Benign lesions of the spleen can easily be diagnosed using current radiologic and histopathologic techniques without the need for surgery[32,33,34].

1.3.1.7. Haematologic Diseases:

The haemolytic anemias are important causes of splenomegaly. They are usually due to intrinsic abnormality of the red cell such as membrane disorders, hemoglobin disorders and enzyme disorders or due to extrinsic abnormalities such as Hereditary Spherocytosis (HS), Thalassemia and Sickle Cell Disease. Children with homozygous Sickle Cell Disease are at risk to develop splenic sequestration until age six years. Parents of infants and toddlers with Sickle Cell Disease need to learn how to palpate the spleen in order to detect splenomegaly as early as possible[35,36].

1.3.2. COMMON CAUSES OF SPLENOMAGELY IN THE TROPICS:

The more common causes of splenomegaly in childhood in the tropics are:

- Infections: like Typhoid Fever, Brucellosis, Relapsing Fever, Typhus, Syphilis, Leptospirosis, Miliary Tuberculosis and Bacterial Endocarditis.
- Intestinal Schistomiasis, Hydatid Disease and Histoplasmosis (duboisii). Hyperactive malarial splenomegaly (HMS) and splenic lymphoma with villous lymphocyte are found as causes of splenomegaly in West Africa.
- Others like Thalassaemia, Sickle Cell Disease, Portal hypertension, Burkitt's Lymphoma, Deficiency anemia and Leukemia[37,38].

1.4. EVALUATION OF PATIENTS WITH SPLENOMEGALY:

Despite the extensive differential diagnosis, a careful history, examination and investigations including cell count and liver function tests often provide a short list of etiologies. The history should cover all symptoms that can give a clue to the diagnosis[39,40].

1.4.1. Chief Symptoms:

The symptoms that can give a clue to the diagnosis include:

Abdominal pain which may indicate a history of abdominal trauma.

History of diarrhea, bone pain, weight loss and fever can give a clue to malignancy such as leukaemia.

Epistaxis or bleeding from any site can give a clue to bleeding disorder[39,40,41].

1.4.2. Past Medical History:

In patient with splenomegaly it is important to consider a history of neonatal sepsis or catheterization, history of jaundice, surgical procedure. History of blood transfusion, known blood disorder such as thalassaemia or a sickle cell disease must be considered[39,41,42].

1.4.3. Family history:

- Anemia and cholecystectomy which may indicate hemolytic anemia-associated gallstones.
- Splenectomy which may suggest the possibility of hemolytic anemia.
- Mediterranean ethnicity with the possible increased incidence of Thalassemia and Glucose -6- Phosphate Dehydrogenase Deficiency.

- African ethnicity and the likelihood of Sickle Cell Anemia and G6PD.
- Haemolysis in male, which may be due to G6PD.There, was considerable overlap in the occurrence of G6PD, Quinine ingestion and Malaria leading to Haemolysis and haemoglobinurea[41,42,43].

1.4.4. Physical Examination:

The spleen is best examined by standing on the right side of the child and palpating the left quadrant of the abdomen with the right hand. The child should be examined in the supine position. Light pressure is preferred in children because the spleen can be easily pushed out without feeling its edge. Percussion over the left lower lateral ribs may reveal splenomegaly that is not evident on palpation. Liver and spleen may also become palpable if pulmonary pathology causing hyperinflation is present[42,43,44].

Important features on examination include the following:

Failure to thrive may suggest the presence of malignancy, chronic hemolysis, liver diseases or inflammatory disease[42,43,44].

Pallor, which may be due to anemia that, may indicate hemolysis or bone marrow infiltration.

Petechiae or purpura that might be caused by thrombocytopenia, which may indicate bone marrow disorder or hypersplenism. Jaundice

which might be caused by hemolytic anemia or liver diseases. Itching which may indicate liver dysfunction.

Skin Rashes, which might be related to acute or chronic infections, (SLE), Infective Endocarditis, Histocytosis, or Hemangioma. Eczema, which may be related to Langerhans cell Histocytosis or Immunodeficiency[43,44,45].

Dyspnoea and fatigability caused by anemia or congestive heart failure. Recently developed murmur, which may indicate Endocarditis[43,44,47].

Abdominal tenderness which might be caused by gallstones, hepatitis or trauma. Abdominal distention, prominent abdominal veins and ascites which are mostly caused by liver disease. Liver size and texture[43,44,45].

Joint pain may be caused by systemic lupus erythematosus or rheumatoid arthritis. Poor bone growth, which might be caused by storage diseases or osteopetrosis. Bones pain such as that is caused by leukemia or Gaucher Disease [43,44,45].

Poor vision which might be caused by Osteopetrosis. Eye examination may reveal uveitis or iritis, which might be caused by sarcoidosis or rheumatoid arthritis. Loss of developmental milestones which might indicate storage disease or chronic infections[43,44,45,48].

1.5. DIFFERENTIAL DIAGNOSIS:

The differential diagnosis of splenomegaly included the following:

Malignancy such as Leukaemias and lymphomas. Portal Hypertension and Tropical Splenomegaly Syndrome. Infections such as Salmonella Infection, Cytomegalovirus Infection, Hepatitis B or C, Endocarditis, Bacterial. Other diseases like Myelofibrosis, Systemic Lupus Erythematosus, Gaucher Disease and Human Immunodeficiency Virus Infection must be considered[43,49,50].

1.6. LABORATORY STUDIES:

Splenomegaly is usually the result of a systemic disease and not the result of a primary splenic disease. Most useful laboratory tests are the complete blood cell count with a differential count, peripheral blood picture and liver function tests:

1.6.1. Complete blood count may demonstrate the following:

- Pancytopenia may be present because of bone marrow infiltration, which may occur with viral infections or massive splenomegaly as what occur in Gaucher Disease[7,41,52].
- The white blood cell count may reveal the presence of atypical lymphocytes, infection or blast cell, which is suggestive of leukemia,

neutropenia or neutrophilia, which may be caused by infection or leukemia.

- Hemoglobin, RBC smears and reticulocyte count may demonstrate anemia or the presence of malarial parasites.
- Platelets count may indicate thrombocytopenia from decreased production or increased destruction which may be due to immunologic causes, drugs reactions, viral infections or sequestration that is caused by splenic pooling of platelets[50,53,54].

1.6.2 Liver Function Tests:

May demonstrate the following abnormal values:

- Hypoalbuminemia, prolonged prothrombin time, indirect and direct hyperbilirubinemia which may suggest liver dysfunction.
- Isolated indirect hyperbilirubinemia which may be due hemolysis.
- Elevated aspartate aminotransferase (AST) and alanine aminotransferase (ALT) which may suggest liver damage.
- Elevated gamma glutamyl transferase (GGT) and alkaline phosphatase[50,55].

1.6.3. Serology:

- Obtain Antinuclear Antibody Titer to screen for systemic lupus.

- Measure immunoglobulin levels, neutrophil function and T-cell subclasses which may be due to Immunodeficiency.
- Viral antibody titers detected for EBV, CMV, Toxoplasmosis and HIV[55,56].

1.6.4. Blood Cultures:

- May reveal the presence of bacterial, fungal, or other infections[55,56].

1.6.5. Bone marrow Examination:

- Perform a bone marrow examination to screen for leukemia, lymphoma, storage disease and disseminated fungal or mycobacteria infections[55,56].

1.6.6. Imaging Studies:

- An ultra sonographic examination can confirm the presence of the enlarged spleen or provide accurate dimensions. Also may distinguish between spleen and other causes of left hypochondrial mass (e.g. Kidney). Splenomegaly can be diagnosed by measuring spleen to left kidney ratio using ultrasound in children age less than 15 years[57,58,59].
- Computed Tomography (CT) scanning and Magnetic Resonance Imaging (MRI) of the abdomen shows the abnormalities of the

spleen size, shape and define parenchymal pathology. MR Imaging is an excellent tool for diagnosing and evaluation of focal lesions and pathologic conditions of the spleen[58,60].

- Radio Isotopic Scanning with a technetium Tc 99m sulfur colloid can provide functional abnormalities, which the radio- logic studies do not provide. Also can provide normal hepatic and splenic size[61].

1.6.7. Histopathologic Findings:

Biopsies of the spleen are rarely obtained. Occasionally a diagnosis depends on it in some infilterative diseases such as Gaucher Disease, Niemann -pick disease, amyloidosis and glycogen storage diseases. Ultrasound-guided splenic biopsy is minimally invasive, simple and safe procedure for use in children. It provides relatively high diagnostic accuracy while minimizing complications when compared with alternative,more invasive procedures [55,56,62].

1.7. TREATMENT:

1.7.1. Medical Treatment:

Because splenomegaly is usually the result of an underlying systemic disease, the treatment is that of the underlying disease. In certain circumstances, splenectomy is the therapy of choice in order to prevent the complication caused by the enlarged organ. The new conjugated vaccines, the older polyvalent pneumococcal vaccine along with haemophilus influenzae vaccine, are indicated to all asplenic children and to those who are about to undergo splenectomy. Daily antibiotic prophylaxis with penicillin is recommended to prevent pneumococcal infection. Antibiotic prophylaxis is often administered for several years after splenectomy[7,50,63].

In patients with homozygous sickle cell anemia or sickle -B thalassemia, oral penicillin must be started after the diagnosis is established and should be administered up to 5 years of age. Febrile illnesses in asplenic children should be approached as potentially life-threatening events. The child should be evaluated thoroughly and treated with intravenous antibiotics[7,35,64,65].

1.7.2. Surgical Treatment:

Splenic trauma is the most common surgical indication for splenectomy. Other causes include splenic cysts, tumors and vascular lesions. Partial splenectomy is preferable to decrease the risk of septicemia, but total splenectomy is occasionally necessary. Splenectomy

can be indicated in patients with Sickle Cell Disease because of recurrent acute splenic sequestration or chronic hypersplenism.

Splenectomy can cure hypersplenism but is not usually indicated. Ali, Salem Ah in 1999 in Saudi Arabia, found that hypersplenism was an indication for splenectomy in 11 patients out of 20 who had massive splenomegaly. They found that with good preoperative management, splenectomy in children with massive splenomegaly is both safe and effective[7,66,67].

Splenectomy may be helpful in improving cytopenias in several medical conditions such as spherocytosis, elliptocytosis or autoimmune disorders such as immune thrombocytopenia. In Thalassemia major splenectomy decreases the transfusion requirement .In a study done in Saudi Arabia the requirements decreased markedly, post operatively, from 18 transfusions/year to only 4 transfusions/year. In Gaucher Disease it may be necessary to avoid mechanical strain of a huge spleen which may require intervention. In children with Sickle Cell Disease splenectomy may be indicated in repeated sequestration crisis in order to prevent recurrences of the crisis[7,35,66,68].

Splenectomy, as a part of an exploratory laparotomy, was once an important component of staging of Hodgkin Disease. This procedure is now infrequently used because of the high risk of post splenectomy sepsis.

Moreover, the increased use of chemotherapy in these patients, which allows treatment, decisions to be made on the basis of radiologic evaluation alone. Further more, some data suggest that splenectomy increases the risk of second malignancy in patients treated for Hodgkin disease[7,35,66,69].

1.7.3. Consultations:

Consultation may require paediatric hematologist/oncologist in the absence of an obvious etiology of splenomegaly or when a primary hematological disorder is suspected[7,35,66,70].

1.7.4. Restriction of activity:

Activity restrictions depend on the degree and etiology of the splenomegaly. Spleen enlargement greater than a tip leaves the spleen more exposed to possible trauma when below the protection of the rib cage. The larger the spleen, the greater the risk of exposure. The American Academy of Pediatrics has listed splenomegaly as a reason to avoid contact sports. In practice, however, many hematologists consider the risk of trauma, splenic size and the underlying cause of splenomegaly in their recommendations regarding activity[7,35,70,71].

Modest degrees of splenic enlargement, such as 2-3 cm below the left costal margin carry a small risk. More risky contact sports, such as football, should probably be avoided. However, baseball may be considered

less risky and permissible if the issue is one of the importances's to the family and they understand the risk[7,35,70,71].

Children with splenomegaly due to acute viral illness, in particular to infections mononucleosis, demonstrate great fragility of the spleen and are at much greater risk of rupture even with more modest degrees of splenomegaly. Their restrictions on contact sports should be more, but this is often not considered as a problem because of the usually self-limited nature of the process[7,35,70,72].

1.7.5. Medications:

The choice of therapy is dependent on the specific etiology of the splenomegaly:

1.7.5.1. Drug category:

- Vaccines:

Active immunization increases resistance to infection. Vaccines consist of microorganisms or cellular components, which act as antigens. Administration of the vaccine stimulates the production of antibodies with specific protective properties with the increased problem of penicillin resistance. In S.pneumonia, prevention by immunization using the conjugated pneumococcal vaccine for children or the unconjugated 23-valent-pneumococcal vaccine for adults is mandatory. Similarly,

immunizations with the conjugated H influenza type b and meningococcal A and C vaccines are essential. Vaccines are administrated at least 10 days before splenectomy.

- Antibiotics:

Daily antibiotic prophylaxis with penicillin is recommended to prevent pneumococcal septicemia[7,33,70,73].

1.7.5.2. Follow-up:

Further care is dependent upon the specific etiology of the splenomegaly and rarely upon the splenomegaly itself. An exception to this is the development of hypersplenism, but the resulting anemia, leucopenia, and/or thrombocytopenia usually are not severe enough to cause serious problems, particularly in children[7,33,70,73].

1.7.6. Complications:

Major complications of splenectomy are overwhelming sepsis with encapsulated bacteria such as strept.pneumoniae, H. influenza and N. meningitides.

The overall risk of sepsis in asplenic patients is approximately 2% but this is variable depending on the age of the patient and the underlying disease. As compared to children with aspleen, the incidence of mortality

from septicemia after trauma is 50 times greater in children who are splenectomized and is 350 times greater in children with sickle cell disease. The risk of sepsis is two times greater in children younger than four years and the rate of sepsis is up to 30% in the first year of life. For this reason, when possible, splenectomy is often delayed in young children. The frequency of sepsis is highest in the first 5 years after splenectomy. The mortality rate due to sepsis in these patients is approximately 30-50%. Therefore, prevention of sepsis is crucial for asplenic patients[7,33,66,70,73].

1.7.7. Prognosis:

The prognosis is dependent on the specific underlying etiology of splenomegaly[7,33,70,73].

1.8. PREVIOUS STUDIES IN SPLENOMEGALY:

1.8.1. Studies done in developed countries:

Zimmerman AS studied the prevalence of palpable splenomegaly in children with hemoglobin SC (Hbsc) disease and to determine the hematological and clinical manifestations of splenomegaly in these patients. A retrospective chart review of 100 patients with Hb SC over two years of age followed by the Duke University pediatric sickle cell program in the United State. Serial physical examinations and laboratory measurements were adopted. Palpable splenomegaly was present in 34% of patients and

was more common in males. Children with splenomegaly had a significantly lower average hemoglobin concentration, 10.3 Vs 10.8 g/dl,p=0.011 and lower platelets count, 237 Vs 314×10^9/L ($p<0.001$) than those without splenomegaly. Children with measurements, both before and after the onset of splenomegaly, had a significant decrease in the platelets count 279 Vs 216×10^9/L, (P<0.001) and white blood cell count 9.1 vs. 7.9×10^9/L, (P=0.04) after splenomegaly was identified. Clinical complications included acute splenic sequestration in 12% of children (medium age 5.4 years) while hypersplenism with chronic thrombocytopenia in another 10% of patients (medium age 10.6 years). Splenomegaly is a common physical finding in children with Hbsc disease and is often associated with mild cytopenias. Clinical complications of splenomegaly include acute splenic sequestration in younger patients and hypersplenism with chronic thrombocytopenia in older children[73].

Bricks, LF and their colleagues in 1993 described children with hepatosplenomegaly attending the General Pediatric Teaching Ambulatory of Institute De Crianca, Sao Paulo, identifying the main causes, evolution, and necessity for hospitalization and/or referral to specialists. Of the 89 children included (age range, 1-148 months), 64 of them (72%) were referred from other services for hepatosplenomegaly investigation. Most common presenting complaints were, fever in 39 children (44%), pallor in

26 children (29%), weight loss in 21children (24%) and jaundice in14 children (16%). Main observations noticed on physical examination were pallor in 47 children (53%) and short stature in 17 children (19%). Anemia was diagnosed in 70 children (79%), 35 children (39%) had infections, seven children (08%) had metabolic disorders and only five children (06%) had neoplastic disorders. The most frequent infections were of the urinary tract, which was found in nine children (10%) and hepatitis A in six children (07%). Thirty-six children 40% were referred to specialists, 17 of who were already diagnosed. The conclusions of the study were that, most of the children with hepatosplenomegaly presented with deficiency anemia associated with infections, which the general pediatrician was able to diagnose. Persistence of unexplained hepatosplenomegaly for more than two months, especially when there was substantial volume enlargement or alteration in the organ consistency, was an indication for referral to specialists [(74)].

Imrie J, Wraith, JE described four patients with Niemann-Pick disease type C (NPC) in Manchester. The presentation was isolated splenic enlargement, which remained the only abnormality for a number of years. Diagnosis can be suggested by either finding abnormal storage material in a tissue biopsy specimen or by showing a modest elevation in plasma chitotriosidase activity. In-patients with suggestive abnormalities, filipin

staining of skin fibroblast samples should confirm the abnormality in cholesterol trafficking. Formal esterification studies and mutation analysis should also be performed, especially if prenatal testing is to be performed in subsequent pregnancies. If the diagnosis is not considered and established, the family are at risk of having further affected children. Investigation of patients with isolated splenomegaly is not complete until (NPC) has been excluded[75].

O' Reilly, RA had studied splenomegaly at a municipal teaching hospital in United State in an 11 years retrospective review. The 170 patients were classified into six diagnostic groups. The associated clinical and laboratory features were tested for statistical association (X^2), to determine predictive values. Hepatic diseases caused 36 of the splenomegaly (21.2%), hematological disorders in 35 of them (20.6%), infectious diseases in16 of them (09.4%), inflammatory conditions in five patients (02.9%), primary splenic diseases in four patients (02.4%) and other disorders in three patients (01.8%). The acquired immunodeficiency syndrome (AIDS) occurred in 54 of the patients with infectious diseases. Hematological diseases were significantly associated with hepatomegaly ($p< 0.01$), abnormal liver function tests (LFT) and blood "cytopenias". Compared with previous reports, both congestive heart failure and endocarditis now rarely cause splenomegaly. All blood cytopenias had

highly significant associations only with hepatic diseases, which suggest that hypersplenism remains a useful concept for the splenomegaly of liver disease[76].

Landing BH and his colleagues studied the splenic growth rates in cirrhotic and other splenomegalic diseases of childhood. The weights of the spleens of series of patients with various disorders of children dating from birth or early infancy and causing splenomegaly with or without cirrhosis of the liver, were analyzed. The linear regression equation for spleen weight versus age in months for each disease was derived, and the rate constants from these equations were adjusted for the age range of the patients in each group. The original data of Coppoletta and Wolbach were used for normal values. The rates of splenic growth of appropriate entities for which the regression equation could be computed fell into three groups. These included the adjusted rate constants, growth of spleen in grams per month, of 6.53-6.95 in biliary atresia, thalassemia and cirrhosis. This is following by neonatal hepatitis, 2.30-2.62 in cirrhosis of alpha -1- antitrypsin deficiency, infantile polycystic disease and spherocytosis and 1.06-1.11 in cystic fibrosis and idiopathic thrombocytopenic purpura. These classes of splenic growth rates are approximately 10, 3.7 and 1.6 times the normal growth rate (0.67 g/mo). Rate constants could not be computed for the categories of cirrhosis following viral hepatitis and hemolytic anemia other than

spherocytosis and sickle cell anemia. However, the number of patients with splenic vein obstruction, cirrhosis with the cholestatic syndrome of parental alimentation, hypoplastic anemia with hemosidrosis, tyrosinemia, Byler's disease, congenital hepatic fibrosis and Wilson's disease were too few for analysis. The significance of the finding of classes or quantum groups of splenic growth rates in disorders of children, dating from birth or early infancy and causing splenomegaly, is uncertain. Comparable data on adequate series of patients with other appropriate disorders will be necessary[77].

Porter, David W and other authors described a rare tumor with overlapping features of true histolytic sarcoma and inter digitating dendritic cell sarcoma occurring in infancy. A three months old boy presented with hepatosplenomegaly and abdominal distension. He presented a diagnostic challenge at initial presentation despite extensive. On follow-up at age 16 months, he had progressive splenomegaly, thrombocytopenia and worsening coagulapthy. A diagnosis was established after an open biopsy of liver and spleen. A conclusion of a repeat liver biopsy coupled with splenic biopsy is recommended in young children with unexplained hepatosplenomegaly and thrombocytopenia[78].

Arya et al had studied the clinicoradiologic features and prognostic significance of splenomegaly and that of splenic involvement in childhood

Hodgkin Disease (HD). One hundred forty-one children presenting with (HD) between January 1991 and February 2001 and treated with chemothengy alone were included in the study. Radiotherapy was given to four patients with resident mediastinal disease. Patients were staged clinically and assessed for splenic deposits by computed Tomography, ultrasonography or both. The results of the study were that, splenic involvement was seen in 22 children (15.6%). On univariate analysis, spleen deposits were significantly correlated with constitutional symptoms (P=0.02), splenomegaly on physical examination (P< 0.001), involvement of three or more lymphnode areas (P=0.006), involvement of subdiaphragmatic lymphnodes (P=0.01), mediastinal involvement and bulky disease (p=0.001). Multivariate analysis retained enlarged spleen, involvement of three or more lymphnodes areas and bulky disease as significant risk factors for spleen involvement. Conclusion of study is that enlarged spleen, involvement of three or more lymphnode areas, and bulky disease are predictable risk factors for (HD) splenic deposits. Splenic involvement on Computed Tomography scan or ultrasonography is significantly associated with relapse and contributes to a poorer outcome of (HD) in children treated with chemotherapy alone[24].

1.8.2. Studies done in developing countries:

1.8.2.1. African countries:

Salma Dahwi in 1996 studied causes of gross splenomegaly in Sudanese adults. The study group was consisted of 95 patients, 77.9% of them were male and 22.1% were female. The study aimed to identify the causes of gross splenomegaly in Sudan and to study the pattern of different diseases and their presentation.

Portal hypertension due to schistosomiasis was found in 32.7%, Visceral leishmaniasis in 27.4%, liver cirrhosis in 9.4%, chronic myeloid leukaemia in 10.5%, chronic lymphoid leukaemia in 10.5%, lymphoma in 4.2% and hyper reactive malarial splenomegaly (TSS) in 3.2%[79].

Greenwood, BM and his colleagues in 1987 studied the ethnic differences in the prevalence of splenomegaly and Malaria in Gambia. They found significant variations among members of the three main ethnic groups resident in North Bank Division. Among young children, splenomegaly and malaria were less prevalent in Mandinkas than in Wollofs or Fulas, suggesting that some genetic or environmental factors protect Mandinka children from this infection. Among older children and adults splenomegaly was found most frequently in Fulas. Six out of twenty two adults (27%) with very large spleens had a high serum IGM level and

probably had the hyperactive malarial splenomegaly syndrome. Four of these six subjects (66.6%) were Fulas. This findings, together with the results of a previous study in Nigeria, suggest that fulas have a predisposition to this condition[80].

Lowenthal, MN reported a result of spleen surveys that had been carried out in various groups in Zambia during the period January 1985 to October 1988. The lowest spleen rates were found in urban workers and in long stay adults in leprosy and psychiatric hospitals. The highest rates were in rural school children and children in a rural hospital. Intermediate between these groups were adults in an urban and in a rural general hospital[81].

Timite, Konan M and their colleagues studied the etiology of splenomegaly in children in the tropics. One hundred and seventy-eight patients seen over a four-year period (1985-1988) at the Cocody Teaching Hospital in Ivory Coast were reviewed. The incidence of splenic enlargement among pediatrics was (1.6%). Males, whose number was 106, were more often affected than females whose number was 72. Slightly over half of the children (54.49%) were 0 to 5 years of age. The main clinical presenting features were fever (90%), anemia (72%), and a decline in general health (36.50%), enlargement of the liver (33.50%), Jaundice (26.50%) and enlarged lymph nodes (07%). Main etiologies included

malaria (53%), Salmonella infections (15%), and sickle cell anemia (14%), Schistosomiasis (09%), AIDS (03%) and Thalassemia (02%). Malignancies like leukemia and lymphoma were relatively infrequent. More than one etiology was found in 13 children. The distribution of etiologies by age group was determined and a strategy for investigating children with splenic enlargement in tropical countries was developed[82].

Mwatha JK and his colleagues studied an association between anti-schistosoma Mansoni and anti-plasmodium falciparum antibody responses and hepatosplenomegaly in Kenyan school children. School children from two areas of Kenya, Kangundo and Kambu, had contrasting prevalence and intensities of Schistosoma Mansoni infection. However, in individual children, S. Mansoni infection intensity is positively correlated with organomegaly. In a previous study, hepatosplenomegaly was associated with certain type of anti schistosome cytokine responses. Although the high-morbidity Kambu area had higher malaria transmission than did the low-morbidity Kangundo , hepatospelenomegaly was not associated with clinical malaria or with patent malarial parasitemia. However, chronic exposure to malaria might be involved. Here, retrospectively, they assayed plasma from this original study, for anti-plasmodium falciparum and anti-S.Mansoni antibodies , to test whether greater exposure to plasmodium was a cofactor for hepatosplenomegaly. They found that hepatosplenic

children had significantly higher levels of anti-P.falciparum antibodies, compared with non hepatosplenic children, a finding that strongly suggests that some experience of P.falciparum influenced the development of hepatosplenomegaly in these S.Mansoni infected children [83].

Mark Booth and his colleagues studied the micro-geographical variation in exposure to S.Mansoni and malaria infections, and exacerbation of splenomegaly in Kenya School-aged children. They concluded that this variation in exposure could be exploited to investigate the chronic impact of these two infections. These results provided firm evidence that relatively high exposure to both infections exacerbates splenomegaly even outside the malaria transmission season [84].

1.8.2.2. Asian countries:

Ali N, Anwar M and their colleagues studied the hematological evaluation of splenomegaly in Combined Military Hospital, Pakistan. They aimed to find out the relative frequency of clinical conditions associated with splenomegaly that require hematological evaluation in their set up. They included patients of both gender and all age groups with palpable spleens. Patients with splenomegaly due to liver diseases, malarial parasites on thick or thin blood film, positive Widal test or positive blood cultures were excluded from the study. Patients were clinically evaluated with clinical history, microscopic examination of blood smear and blood counts.

Depending upon provisional diagnosis bone marrow examination or investigations for hemolytic anemia were performed. In the result they found that one hundred patients were involved. Seventy-eight patients were adults and twenty-two patients were of pediatric age group. In the adults, hematological malignancies were seen in 37%, malarial parasites in bone marrow in 20.5%, megaloblastic anemia in 13%, bacterial infections in 09%, hemolytic anemia in 09%, tropical splenomegaly in 05% and a positive bone marrow culture for salmonella in 06.5%. In children, hematological evaluation revealed hematological malignancies in 18%, beta thalassaemia in 55%, other hemolytic anemias in 13.5%, congenital sidrobalstic anemia in 04.5% and storage disorder in 09%. The conclusion of the study was that: hematological workup was more informative in most of the cases. Bone marrow examination is the key investigation. Hematological malignancies constituted 37% of the adults and 18% of pediatric age group patients while hemolytic anemia constituted 68% of pediatric age group [(85)].

Zeinat Hijazi, Zahra Qabzard and others had studied the splenomegaly in Arab Children with Idiopathic Thrombocytopenic Purpura. They found that in 31out of 56 Arab children (55%) with idiopathic thrombocytopenic purpura, splenomegaly was present. Of those with splenomegaly, 84% had evidence of iron deficiency anemia compared to 48% in those without splenomegaly. There was no significant difference in

the prevalence of B-thalassemia trait or history of preceding viral infection between those with or without splenomegaly. This study demonstrated a much higher prevalence of splenomegaly in Arab children with idiopathic thrombocytopenic purpura, most probably related to associated iron deficiency. Splenomegaly is reported in about 10% of children with Idiopathic Thrombocytopenic Purpura (ITP). Its presence in a child with thrombocytopenia usually suggests a more serious underlying disease such as leukemia. In a retrospective analysis of fifty-six Arab children with ITP, a much higher incidence of splenomegaly was found. This report explains this observation and correlates it with the presence or absence of anemia [(86)].

Ghosh K, Mukherjee studied splenomegaly in School Children in a remote tribal area of Dhole district, Maharashtra. A total of 480 schoolchildren were clinically examined for splenomegaly and a history of typical malaria fever and/or blood slide positivity for malaria in the past two years. About 09.55 percent of normal population had either splenomegaly or convincing history of malaria infection in the past two years which was not statically different from the Sickle Cell Trait patients having evidence of past malaria 8.79 percent [(87)].

JUSTIFICATIONS AND OBJECTIVES

- Splenomegaly is a common clinical finding that is associated with various diseases in Sudanese children.
- Children with enlarged spleen in tropical areas need a certain protocol for investigations to reach a possible diagnosis.
- No similar study has been done in Sudan in children.
- To study the causes of splenomegaly and the common presenting features in children who were admitted to hospital and seen in the referred clinics.
- To study the investigations done for children with splenomegaly in different paediatrics hospitals.

Chapter Two

2. PATIENTS AND METHODS

2.1. Study design:

This is a crossectional, descriptive, hospital based study.

2.2. Study area:

The study was conducted in all Khartoum State Paediatrics Emergency Hospitals (wards and referred clinics). The main hospitals included in the study are the following:

- Khartoum Teaching Hospital.
- Gaafar Ibn Auf Children Emergency Hospital.
- Soba University Hospital.
- Omdurman Children Emergency Hospital.
- Ahmed Gasim Paediatrics Hospital.

2.3. Duration of the study:

The study was conducted during the period (February 2005 – July 2005).

2.4. Study population:

The study included children in the age group (0 - 16) years, who had splenomegaly and were admitted to the paediatrics wards or came for follow up in the referred clinics of these hospitals.

2.5. Sample size:

The sample size, 217, was selected randomly and calculated according to the formula:

$$N = \frac{Z^2(Pq)}{d^2}$$

N = sample size d = degree of accuracy

Z = (standard normal device) 1.96(95%).

P = prevalence or the probability of the problem under study (88).

2.6. Inclusion criteria:

All children in the age group (0 - 16) years and had splenomegaly who presented to the study area and were admitted to the wards or seen in the referred clinics.

2.7. Exclusion criteria:

- Refusal of parents or patients to participate in the study.
- Patients in whom certain investigations could not be done because of unaffordability or unavailability in the hospitals.

2.8. Study technique:

2.8.1. Ethical consideration:

Verbal consent was obtained from the consultants of the pediatrics units in the above mentioned hospitals and from parents of the children included in this study.

2.8.2. Study tools:

2.8.2.1. Questionnaire:

A standardized questionnaire sheet was designed which included the personal characteristics such as name, gender, ethnic groups, schooling, performance and age which was divided into four groups. These groups were 0-<1 year, 1-<5 years, 5-<10 years and 10-16 years.

It also provided the demographic characteristics of the father and mother such as occupations, the level of education and consanguinity. Also it included information about vaccination of the child, past medical history of blood transfusion, abdominal trauma, vomiting of blood, Schistosomiasis, umbilical catheterization or sepsis and history of jaundice. Moreover, it included the investigations that were performed along with the final diagnosis. Treatment offered to these patients and the out come were also included.

2.8.2.2. Clinical examination:

Every child included in the study was subjected to a thorough clinical examination, with emphasis on the presence or absence of pallor, Jaundice, petechial or purpuric rash, lymphadenoapthy, abdominal distension and visible dilated veins of the abdomen, enlargement of liver. The enlargement of the spleen (splenomegaly) was graded into five grades:-

- grade I : Just palpable spleen.
- grade II: mild splenomegaly in which the spleen is enlarged down to the midway between the left costal margin and the umbilicus.
- grade III : moderate splenomegaly in which the spleen is enlarged down to the umbilicus.
- grade IV : huge splenomegaly in which the spleen is enlarged down to midway between the umbilicus and pelvic brim.
- Grade V : massive splenomegaly in which the spleen is enlarged down to the pelvic brim.

This grading of splenomegaly depends on anatomical marks. There are no specific metric measurements used here. Measuring the size of the spleen by centimeters differs from child to child according to age and it will not give us the clinically significant size of the spleen. This is unlike the classification that was prescribed by Hackett which is useful in community based surveys [90].

2.8.2.3. Investigations

2.8.2.4. General investigations:

These included the investigations that were done to all children who presented to the study area for the first time was recorded. For those who were seen in the referred clinics, the most recent investigations were taken as they were and recorded. The investigations that were done in the hospital where the child was admitted were sensibly designed. They included the following:

- Complete Blood Count (CBC), which included ESR, platelets count and peripheral blood picture. They were done according to the standard methods and registered with reference to the Sudanese children normal values.
- Blood film for malaria for all children presented to the study area.
- Urine general for all children, and specifically for ova of Schistosoma Haematobium for whom Schistosomiasis was suspected.
- Stool general for all children and specifically for ova of Schistosoma Mansoni. This was tested by concentration method for three consecutive days.
- Abdominal Ultrasound was done to majority of patients to confirm the enlargement of the spleen and to give a clue for diagnosis.

2.8.2.5. Investigations done when requested:

These included the investigations, which were indicated according to the presenting condition of the child. These included:

- Bone marrow aspiration and/or trephine biopsy and it was done by using standard methods.
- Sickling test for those who were suspected to have Sickle Cell Disease, done by using the standard method.
- Hb electrophoresis for those who were suspected to have haemoglobinopathies, done by using the standard method.
- Liver function tests for those who were suspected to have any effects on their liver function from the underlying disease.
- Mantoux test by using the purified protein for those who were suspected to have tuberculosis.
- Widal test for Enteric Fever or Brucellosis by using the standard methods for those who were suspected to have Typhoid Fever or Brucella infection.
- Lymph node biopsy was done for histopathology by the standard method for those who required further confirmation of their disease.

2.8.3. Classification of socio-economic status:

This was classified according to the Father's and Mother's occupation into:

- Class I (high social class): The professionals and business- men.
- Class II (moderate social class): The government employee, skilled labourers and the small scale businessmen.
- Class III (low social class): The unskilled labourers and unemployees.

2.8.4. Ethnic groups:

Each tribe in the study group was referred to its original ethnicity that has been done by Elshareefs in his book about classification and origin of common Sudanese tribes and non Sudanese tribes. Accordingly the tribes here were classified into Nubians, Arabs, Bija, Nuba, Baggara, Nilotics, Kordofanian and Darfurian. The questionnaire was filled by the author and registrars on duty.

2.8.5 Outcome:

The outcome of the study group was evaluated as regard to the complete recovery, improvement; mortality and recording those who were lost for follow up from their respective units for various reasons.

2.9. Data analysis:

All data was analyzed using (SSPS). Descriptive frequencies were obtained for all variables. Chi square tests were measured for selected variable. The level of significance was taken as $P < 0.05$.

2.10. Potential difficulties:

The potential difficulties in this study included:

- The difficulties in follow up of some patients who were living outside Khartoum and some times had come to Khartoum only for treatment.
- The poor socio-economic status of the families and lack of adequate hospital facilities to perform certain required investigations.
- The difficulties in transporting some patients for some specific investigations that were done outside their main hospitals. The cost of some investigations, which could not be afforded by the parents.

2.11. Other participants in the study:

The other participants who helped a lot in this study were my colleagues in different pediatrics wards either by calling me for new admitted patients or helping me to carry on with investigations.

2.12 Input of the Author:

- Team leader.
- Filling the questionnaire.
- Taking the history and examination of the patients.
- Follow up of the patients at the referred outpatient clinics.
- Doing some investigations to reach a possible diagnosis, which were difficult to arrange and some times costly to conducted.

2.13 Funds and grants:

The research was done with self-resources without external funds.

Chapter Three

3. RESULTS

A total of 217 children were enrolled in this study, all of them undergone a detailed history and a thorough physical examination.

3.1 Demographic characteristic of the study group:

3.1.1 Age distribution of the study group:

The age of the 217children in the study group ranged from 0–16 years. They were classified into 4 groups. The majority of them, 65 patients (30.0%) were in the age group 10 - 16 years,61 patients (28.0%) were in the age group 5 - < 10 years, 57 patients (26.3%) were in the age group 1 - <5 years while 34 patients (15.7%) were in the age group 0 - <1 year as shown in [Fig. 1].

3.1.2 Gender distribution of the study group:

There was an obvious male predominance in this study, where males constituted 135 patients (62.2%) of the study group while the females constituted 82 patients (37.8%). That gave a male to female ratio of 1.7:1 as shown in [Fig. 2].

3.1.3 Ethnic group distribution of the study group:

Most of the children in the study group were Arab in ethnicity, 90 patients (41.5%), followed by Kordufanian and Darfourian tribes in 47 patients (21.7%). Baggara tribes in 35 patients (16.1%), Nuba tribes in 19 patients (08.8%), Nioltics in 12 patients (05.5%), Nubian tribes in 09 patients (04.1%), while Bija tribes in 05 patients (02.3%) as shown in [Fig. 3].

3.2 Family and social history:

3.2.1 Consanguinity between parents of children in the study group:

Regarding consanguinity between parents of children in the study group, 120 parents (55.3%) were first degree cousins, 28 parents (12.9%) were second degree cousins, 39 parents (18.0%) were far relative, while 30 parents (13.8%) were not consanguineous as shown in [Fig. 4].

3.2.2 Parents educational level:

Considering parents education, most of the fathers, 135 (62.2%), were illiterate. Thirteen fathers (06.0%) attended khalwa, 38 fathers (17.5%) primary school educated, 24 fathers (11.1%) had high school education, and six fathers (02.7%) were university

graduate, while only one father (0.5%) had post graduate education. Regarding mothers education, 142 mothers (65.4%) were illiterate, 42 mothers (19.4%) had primary school education, 24 mothers (11.1%) were educated up to higher secondary school, and seven mothers (03.2%) were university graduate, while two mothers (0.9%) had attended khalwa as shown in [Fig. 5].

3.2.3 Parents occupations:

Considering fathers occupation, seven of them (03.2%) were professional, two of them (0.9%) were businessmen, 18 of them (08.3%) were small scale businessmen, 19 of them (08.8%) were government employee, and 28 of them (12.9%) were skilled labourer. The majority of fathers, 131 (60.4%), were unskilled labourer, while 12 of them (05.5%) were unemployed, including three who had died as shown in {Table 1}.

Regarding the mothers occupation, 204 mothers (94.0%) were housewifes, three mothers (01.4%) were professional, eight mothers (03.6%) were unskilled labourer, one mother (0.5%) was a skilled labourer and another one (0.5%) was small scale businesswomen as shown in [Table. 2].

Table (1) : Distribution of Fathers occupation in the study group (n=217)

Occupation	**Frequency**	**Percent %**
Professional	07	**03.2**
Business men	02	**00.9**
Small scale businessmen	18	**08.3**
Government employee	19	**08.8**
Skilled labourer	28	**12.9**
Un skilled labourer	131	**60.4**
Un employee	12	**05.5**
Total	217	**100.0 %**

Table (2) : Distribution of Mothers occupation in the study group (n=217)

Occupation	Frequency	Percent
H.wife	204	**94.0**
Professional	03	**01.4**
Small scale business women	01	**00.5**
Skilled labor	01	**00.5**
Un skilled labor	08	**03.6**
Total	217	**100.0 %**

3.2.4 Socio-economic status:

Regarding the socio-economic status of children in the study group, 172 children (79.3%) were of low social class while four children (20.7%) were of moderate social class. No children belonged to the upper social class as shown in [Fig. 6].

3.2.5 Family history of anemia:

Regarding family history of anemia among the studied group, 39 of them (18.0%) had positive family history of anemia while the majority of

them 178 children (82.0%) had no family history of anemia as shown in [Fig.7].

3.3 Children education level:

3.3.1 School attendance:

Considering the education of the children in the study group 147 children (67.7%) were not attending school, 41 children (18.9%) were regular attendant, 25 children (11.5%) were irregular attendant while only four children (01.9%) had repeated the year as shown in [Fig. 8].

3.3.2 School performance:

Regarding the 70 children who were attending the school, the performance of three of them (04.3%) was excellent. Good performance was detected in 31 children (44.3%), average performance in 18 children (25.7%) while the poor performance was also detected in 18 children (25.7%) as shown in [Fig. 9].

3.4 Vaccination:

The majority of patients, 144 patients (66.4%), were vaccinated up to date, 32 patients (14.7%) were partially vaccinated while 41 patients (18.9%) were not vaccinated at all as shown in [Fig. 10].

3.5 Symptoms:

Regarding the main presenting symptoms of the study group, fever was found to affect the majority of the patients 209 (96.3%), followed by abdominal pain in 121 patients (55.8%).

Abdominal distension was found to be a presenting symptom in 104 patients (47.9%). Bone pain in 71 patients (32.7%), weight loss in 69 patients (31.8%), general ill health in 104 patients (47.9%), cough and shortness of breath in 61 patients (28.1%). Epistaxis was found in 31 patients (14.3%) while vomiting of blood was found in four patients (01.8%). Jaundice was found to

was found in four patients (01.8%). Jaundice was found to be a presenting complaint in 20 patients (09.2%). Other symptoms such as joint swelling, lower limb swelling, skin rash, diarrhoea, haematuria and convulsions were found in eight patients (03.7%), nine patients (04.1%), six patients (02.8%) two patients (0.9%), one patient (0.5%) and two patients (0.9%) respectively. These symptoms were associated with the main complaint as shown in [Table. 3].

3.6 Signs:

The main signs that were found in the study group were the following: General ill look in 214 patients (98.6%) while unwell look was found in three patients (01.4%). Pallor was found in 182 patients (83.9%) while jaundice was found in 51 patients (23.5%). Forty five patients (20.7%) were found to have lymphadenopathy, Dysponea was found in 69 patients (31.8%), heart murmurs was heard in 40 patients (18.4%) while wheezes or rhonchi in 37 patients (17.1%).Abdominal distention was found in 164 patients (75.6%).Visible dilated abdominal veins was detected in 11 patients (05.1%), abdominal tenderness in 16 patients (07.4%). Hepatomegaly was found in 198 patients (91.2%), ascites in 11

Table (3) : Distribution of the main presenting symptoms in the study group (n=217)

Symptom	Frequency	Percent %
Fever	209	**96.3**
Abdominal pain	121	**55.8**
Abdominal distension	104	**47.9**
General ill health	104	**47.9**
Bone pain	71	**32.7**
Weight loss	69	**31.8**
Cough & S.O.B	61	**28.1**
Epistaxis	31	**14.3**
Jaundice	20	**09.2**
Lower limb swelling	09	**04.1**
Vomiting of blood	04	**01.8**
Skin rash	06	**02.8**
Joint swelling	08	**03.7**
Diarrhea	02	**00.9**
Convulsions	02	**00.9**
Haematurea	01	**00.5**
L.L. swelling	09	**04.1**

patients (05.1%) and lower limb oedema in 13 patients (06.0%).The grades of splenomegaly was found as follow:

Just palpable spleen was found in 40 patients (18.4%), mild splenomegaly in 88 patients (40.6%), Moderate splenomegaly in 69 patients (31.8%), huge splenomegaly in 18 patients (08.3%) while massive splenomegaly in only two patients (0.9%) as shown in {Figure 11}. Other associated findings were petechial or purpuric rash in nine patients (04.1%), Itching in one patient (0.5%), Eczema in one patient (0.5%) and clubbing of fingers in six patients (02.8%) as shown in [Table. 4].

3.6.1 Correlation between the grades of splenomegaly and the age of the patients:

It was found that the most common grade of splenomegaly was the mild one in 88 patients (40.6%), affecting mainly children in the age group 5 - <10 years (34.1%).This was followed by moderate splenomegaly in 69 patients (31.8%), affecting mainly children in age group 10 - 16 years (43.5%). Just palpable spleen was detected in 40 patients (18.4%) affecting mainly children in age group 1 - <5 years (37.5%), huge splenomegaly in 18 patients (8.3%) affecting mainly children in the age group 10 - 16 years (55.6%) while massive splenomegaly was detected in only

Table (4) : Distribution of the main clinical signs in the study group (n=217)

Sign	**Frequency**	**Percent %**
Looks ill	214	**98.6**
Pallor	182	**83.9**
Hepatomegally	198	**91.2**
Abdominal distension	164	**75.6**
Dysponea	69	**31.8**
Jaundice	51	**23.5**
Lymphadenopathy	45	**20.7**
Heart murmurs	40	**18.4**
Wheeze or rhonchi	37	**17.1**
Abdominal tenderness	16	**07.4**
L.L Oedema	13	**06.0**
Visible dilated veins	11	**05.1**
Ascites	11	**05.1**
Petechial or purpuric rash	09	**04.1**
Clubbing	06	**02.8**
Joints deformity	04	**01.8**
Itching	01	**00.5**
Eczema	01	**00.5**

two patients(0.9%) affecting children in age group < 5 years as shown in [Table 5].

3.7. Investigations:

3.7.1. General investigations:

General investigations were done to 217 patients who included:

- Hemoglobin level (Hb), was found less than 10gm/dL in 184 patients (84.8%) which was considered as low level. A level between 10 – 15g/dl was found in 32 patients (14.7%) which was considered as normal level while a level more than 15gm/dL was found in only one patient (0.5%) which was considered as high level as shown in [Figure 12].
- Considering the White Blood Cells Count, the majority of the patients, who were 140 patients (64.5%), were found to have a range between $300\times10^{3/}$ML – $900\times10^{3/}$ML which was considered as normal count. In 44 patients (20.3%) it was found to be > 900×10^{3}ML which was considered as high count while 33 patients (15.2%) had a count less than

Table (5) :Correlation between grades of splenomegaly and Age of children in the study group (n=217)

AGE (years)	GRADES OF SPLENOMEGALY										Total	
	J. palpable		Mild		Moderate		Huge		Massive			
	NO	**%**	**NO**	**%**	**NO**	**%**	**NO**	**%**	**NO**	**%**	**NO**	**%**
0 - < 1	07	**17.5 %**	15	**17.0 %**	11	**15.9%**		**%**	01	**50 %**	34	**100**
1 – 5	15	**37.5 %**	**26**	**29.6 %**	12	**17.4 %**	03	16.6 %	01	**50%**	57	**100**
5 - < 10	10	**25.0 %**	30	**34.2%**	16	**23.2 %**	05	27.5 %	**1**	.0 %	61	**100**
10 - 16	08	**20.0 %**	17	**19.3%**	30	**43.5 %**	10	55.6 %	**1**	.0 %	65	**100**
Total	40	**18.4%**	88	**40.6%**	69	**31.8%**	18	08.3%	**1**	0.9%	217	**100.0%**

$X^2 = 8.823$ P = 0.003

300×10^3ML which was considered as a low count as shown in [Figure 13].

- Regarding the platelets count, 157 patients (72.4%) had normal platelet counts; the range of the count was between 150 – $450\times10^{3/}$ML. The low count, less than 150 $x10^{3/ml}$, was found in 58 patients (26.7%) while only two patients (0.9%) had a high count exceeding 450×10^3ML as shown in [Table. 6].
- The peripheral blood picture was found to be normal in 38 patients (17.5%) and 15 patients (06.9%) had pancytopenia.Abnormality in the RBCs shape and size was noticed among 96 patients (44.3%) while 68 patients (31.3%) had abnormality in the morphology of both the RBCs and the WBC as shown in [Table. 7].
- Blood film for malaria was found to be positive in 34 patients (15.7%) while 183 patients (84.3%) had a negative blood film as shown in [Fig. 14].

Table (6) : Distribution of the platelets count in the study group (n=217)

Platelet count X10 $^{3/\mu l}$	Frequency	Percent %
Low < 150	58	**26.7**
Normal 150 - 450	157	**72.4**
High > 450	02	**0.9**
Total	217	**100 %**

Table (7) : Distribution of the Peripheral blood picture in the study group (n=217)

Peripheral blood picture (P.B.P)	Frequency	Percent %
Abnormal size and shape of RBCs	96	**44.3**
Abnormal morphology of RBCs and WBC	68	**31.3**
Pancytopenia	15	**06.9**
Normal P.B.P	38	**17.5**
Total	217	**100.0 %**

3.7.2 Specific investigations:

- Stool general was done for all patients, in eight of them (03.7%) the stool specimen showed ova of Schistosoma Mansoni while 209 patients (96.3%) had a normal stool specimen.
- Urine examination which was done for all patients revealed the presence of ova of Schistosoma Haematopium in only two patients (0.9%).
- The Sickling test was done for 117 patients, who were suspected to have sickle cell anemia, 38 of them (67.5%) were found to have a positive sickling test while 79 patients (32.5%) had a negative test as shown in [Fig. 15].
- Hb electrophoresis was done for 86 patients, 44 of them (51.2%) had an abnormal electrophoresis while 42 of them (48.8%) had a normal electrophoresis. Regarding those who had the abnormal elecrophoresis, 38 of them (86.4%) had SS HB while six of them (13.6%) had AS HB.
- The Mantoux test was done to 108 patients, nine of them (08.3%) found to have a positive test while 99 of them (91.7%) had a negative test as shown in [Fig. 16].

The Liver Function Test (LFT) was done to 204 patients; six of them (02.8%) had an abnormal L.F.T such as increased total bilirubin, increased serum enzymes and decreased serum protein. One hindered ninety eight of them (91.2%) had a normal L.F.T.

- Abdominal Ultrasound was done to 198 patients, 178 of them (89.9%) had an enlarged spleen with normal texture, 11 of them(05.6%) had an enlarged spleen with abnormal deposits , one of them(0.5%) had an enlarged spleen with coarse texture and eight of them (04.0%) showed a periportal fibrosis as shown in [Fig. 17].
- Bone marrow aspiration was done to 109 patients, 58 of them (55.2%) had a normal active marrow while 23 of them (11.9%) had a hyperactive marrow. Thirty two patients (29.4%) had an abnormal infilteration of their bone marrow like blast cells or L.D bodies while six patients (05.5%) had a depressed marrow as shown in {fig 18}.

3.7.3 Correlation between the grades of splenomegaly and Hb level in the study group:

We found that the grade of splenomegaly correlated significantly with the Hb level (p = 0.002). The two patients with massive splenomegaly (0.9%) had a low Hb level (less than 10 gm/dL). The 18 patients with huge splenomegaly (08.3%) had a low Hb level. less than 10 gm/dl.

The 69 patients with moderate grade splenomegaly (31.8%), most of them 63 patients (91.0%), had low Hb level while six of them (08.7%) had a normal Hb level (10 – 15 gm/dL). The 88 patients(40.6%) who had mild grade splenomegaly, 71 of them (80.7%) had a low Hb level, 16 of them (18.2%) had a normal Hb level while only one of them (01.1%) had a high Hb level (>15gm/dL). The just palpable splenomegaly was detected in 40 patients(18.4%), 30 of them (75.0%) had a low Hb level while 10 of them (25.0%) had a normal Hb level as shown in [Fig. 19].

3.7.4 Correlation between the grades of splenomegaly and WBC count:

The only two patients with massive splenomegaly (0.9%) showed a low count of white blood cells in only one patient (50.0%). The other one patient showed a normal count of white blood cells (300 – 900 × $10^3 ML$). The 18 patients with huge splenomegaly (08.3%) had shown a low white blood cell count (less than 300×$10^3 ML$) in 10 patients (55.6%).The normal white cell count was found in six patients (33.3%) while only two patients(11.1%) showed a high white cell count (more than 900×$10^3 ML$). Patients with moderate grade splenomegaly were 69 patients (31.8%), 41 of them (59.4%), had a normal white cells count, 17 patients (24.6%) had a high count while 11 patients (16.0%) had a low count. The 88 patients(40.6%) who had mild grade of splenomegaly, 66 of them (75.0%) had a normal count, 16 patients (18.2%) had a high count while only six patients (06.8%) had a low count. Patients with just palpable spleen were 40 patients (18.4%) of whom 26 patients (65.0%) had a normal count; nine of them (22.5%) had a high count while only five patients (12.5%) had a low count as shown in [Fig. 20].

3.7.5 Correlation between the grades of splenomegaly and the platelets count:

This correlation was found to be significant (p = 0.00). The only two patients with massive splenomegaly (0.9%), one of them (50.0%) had a low platelets count (< $150\times10^3 ML$) while the other one had a normal platelets count. Regarding the 18 patients with huge splenomegaly (8.3%) nine of them (50.0%) had a low platelets count while the other nine (50.0%) had a normal count. The 69 patients with moderate splenomegaly (31.8%), 36 of them (52.0%) had a normal platelets count while 33 of them (48.0%) had a low count. The 88 patients with mild splenomegaly (40.6%) had a normal platelet count in the majority of them, 76 (86.4%), while a low count was found among 11 patients (12.5%). High platelets count (> $150\times10^3 ML$) found in only one patient (01.1%). The majority of the 40 patients (18.4%) with just palpable spleen who were 35 patients (87.5%) had a normal platelets count while only four patients (10.0%) had a low count High count was found in only one patient (02.5%) as shown in [Fig. 21]

3.7.6 Correlation between the grades of splenomegaly and the peripheral blood picture:

This correlation had been found to be highly significant ($p < 0.00$). In the only two patients with massive splenomegaly, one of them (50.0%) had pancytopenia and the other one (50.0%) had an abnormal shape and size of the RBCs such as microcytic hypochromic cells. The 18 patients with huge splenomegaly (08.3%), eight of them (44.4%) had an abnormal morphology of both the RBCs and WBC in the peripheral picture, five patients (27.8%) had pancytopenia, four patients (22.2%) had an abnormal size and shape of the RBCs while only one patient (05.6%) had a normal peripheral blood picture. The 69 patients with moderate splenomegaly (31.8%), 2 of them (46.4%) had an abnormal morphology of the RBCs and the WBC, 20 of them (29.0%) had an abnormal shape and size of the RBCs only, nine patients (13.0%) had a normal peripheral blood picture and eight patients (11.6%) had pancytopenia. Patients with mild splenomegaly were 88 patients (40.6%), 48 of them (54.6%) had an abnormal shape and size of the RBCs only, 20 patients (22.7%) had an abnormal morphology of the RBCs and the WBC, 19 patients had a normal peripheral blood picture while only one patient (01.1%) had pancytopenia. The 40 patients with just palpable spleen (18.4%),

23 of them (57.5%) had an abnormal shape and size of the RBCs only, nine patients (22.5%) had a normal peripheral blood picture while eight patients (20.0%) had an abnormal morphology of both the RBCs and the WBC. No patient with just palpable spleen had pancytopenia as shown in [Table 8].

3.8 Causes of splenomegaly in the study group:

The causes of splenomegaly in those patients who were able to complete the investigations which was available in the hospitals in the study area, was found to be as follow: Haemolytic anaemias 48 patients (22.1%). This included Sickle Cell Disease, Thalassemia, G6DP and Auto Immune Haemolytic Anemia. Sickle Cell Disease was found in 38 patients (79.1%) of haemolytic anemias. Malaria was diagnosed in 23 patients (10.6%), Schistosomiasis in 11 patients (05.2%), Visceral Leishmaniasis in 13 patients (06.0%) and Tuberculosis in nine patients (04.1%). Malignancies like leukaemias were diagnosed in 15 patients (06.9%) including Acute lymphoblastic, myeloblastic and chronic Leukaemia. Lymphoma was diagnosed in eight patients (03.7%).

Table (8) : Correlation between the grades of splenomegaly and the peripheral Blood Picture among the study group (n=217)

GRADE OF SPLENOMEGALY	PERIPHERAL BLOOD PICTURE								*Total*	
	Abnormal RBCs only		**Abnormal RBCs+WBC**		**Pancytopenia**		**Normal PBP**			
	No	**%**	**No**	**%**	**No**	**%**	**No**	**%**	**No**	**%**
Just palpable	23	**57.5 %**	08	**20.0%**	00	**0.0%**	09	**22.5%**	40	**18.4%**
Mild	48	**54.5 %**	20	**22.7%**	01	**01.7%**	19	**21.6%**	88	**40.6%**
Moderate	20	**29 %**	32	**46.4%**	08	**11.6%**	09	**13.0%**	69	**31.81%**
Huge	04	**22.2 %**	08	**44.4%**	05	**27.8%**	01	**05.6%**	18	**08.3%**
Massive	01	**50 %**	00	**00.0%**	01	**50.0%**	00	**00.0%**	02	**00.9%**
Total										

$X^2 = 49.55$ P = 0.000

- Other diseases included rare disease such as Gaucher Disease, was diagnosed in one patient (0.5%), Hypothyroidism in one patient (0.5%), chronic (ITP) in one patient (0.5%) and systemic lupus erythematosus in one patient (0.5%).

- No definite diagnosis could be reached in 27 patients (12.4%) inspite of full investigations that were done to them as shown in [Table. 9].

3.8.1 Correlation between the causes of splenomegaly and the age group:

- Among the 23 patients who were diagnosed as malaria, nine patients (39.1%) were in the age group 1 < 5 years, 6 patients (26.1%) in the age group 0 - < 1 year as well as in the age group 5 - < 10 years while only two patients (08.7%) in the age group 10 - 16 years

- Schistosomasis was found in 11 patients (05.2%),nine of them (81.8%) were in the age group 10 – 16 years while only two patients (18.2%) in the age group 5-<10 years. No patients with Shistosomiasis in the age group less than five years.

Table (9) : Distribution of the causes of splenomegaly in the study group (n=217)

Causes	Frequency	Percent
Malaria	23	**10.6**
Schistosomiasis	11	**5.1**
Visceral leishmania	13	**6**
Tuberculosis	9	**4.1**
Haemolytic anemia	48	**22.1**
Leukaemia	15	**6.9**
Lymphoma	8	**3.7**
Cardiac diseases	22	**10.1**
Iron Def. Anaemia	7	**3.2**
Liver diseases	5	**2.3**
Tropical splenomegally	8	**3.7**
Myelofibrosis	2	**0.9**
Other infectious diseases	15	**6.9**
Other diseases	4	**1.8**
Un diagnosed	27	**12.4**
Total	217	**100 %**

- Visceral leishmaniasis was reported in 13 patients (06.0%), five of them (38.4%) in the age group10-16 years, four patients (30.8%) in the age group 5 --<10 years as well as in the age group 1 -<5 years. No cases were found in the age less than one year. Tuberculosis which was reported in nine patients (04.1%), was found to affect the whole age groups. Three patients (33.3%) in the age group 10-16 years as well as the age group 5-<10 years. Two patients (22.2%) in the age group 1-<5 years while only one patient (11.2%) in the age group 0-<1 year.

- Concerning haemolytic anaemias which were found in 48 patients (22.1%), 20 of them (41.7%) were in the age group 1 < 5 years. Eleven patients (22.9%) were in the age group 5 < 10 years, 10 patients (20.8%) were in the age group less than one year while seven patients (14.6%) were in the age group more than 10 years of age.

- Leukaemias were diagnosed in 15 patients, six of them(40.0%) were in the age group 10-16 years as well as in the age group 5-<10 years. Three patients (20.0%) were in the age group 1-<5 years. No reported cases of Leukaemia in the age group less the one year. Lymphomas were diagnosed in eight patients (03.7%); six of them (75.0%) were in the age group 5 - < 10 years. One patient (12.5%)

was found in the age group 10---16 years as well as in the age group 1-<5 years. No reported cases in the age group less than one year.

- Cardiac diseases were diagnosed in 22 patients (10.1%), affecting the whole age groups. The majority of them, 11 patients(50.0%), were in the age group 10 – 16 years followed by five patients(22.7%) in the age group 1-<5 years. Four patients (18.2%) were in the age group 5-<10 years while only two patients (09.1%) in the age group 0-<1 year.

- Iron deficiency anaemia was diagnosed in seven patients (03.2%), three of them (42.8%) were found in the age group 5 - < 10 years. Two patients (28.6%) were found in the age group 10-16 years while the other two (28.6%) were in the age group 1-<5 years.

- Liver diseases were diagnosed in five patients (02.3%), three of them (60.0%) were found in the age group 0-<1 year. Two patients (40.0%) were found in the age group 10-16 years. No cases were reported in the age group 5-<10 years as well as in the age group 1-<5 years.

- Tropical splenomegaly was considered as a cause of splenomegaly in eight patients (03.7%); six of them (75.0%) were in the age group 10-16 years. One patient (12.5%) were in the age group 5-<10 years as well as in the age group 1-<5 years.

- Myelofibrosis was diagnosed in two patients (0.9%), one of them (50.0%) was in the age group 5-<10 years while the other one (50.0%) in the age group 10-16 years.

- Other infectious diseases such as Typhoid fever, Pneumonia, Bacterial meningitis, Infectious mononucleosis and HIV were found to affect 15 patients (06.9%).Five patients (33.3%) were found in the age group less than one year, three patients (20.0%) were in the age group 1 - < 5 years, four patients (26.7%) in the age group 5 - < 10 years and three patients (20.0%) in the age group 10 - 16 years.

- The distribution of other rare diseases causing splenomegaly was also recorded in four patients (01.8%). Gaucher Disease was diagnosed in one patient (25.0%) in the age group 1-< 5 year and hypothyroidism in one patient (25.0%) in the age group less than one year (25.0%).One patient (25.0%) was diagnosed as (SLE) in the age group 5 < 10 years and the last one was diagnosed as chronic (ITP) in the same age group.

- Regarding the undiagnosed patients, they were found to be 27 patients (12.4%), six of them (22.2%) were in the age group less than one year, and another six patients (22.2%) were in the age group 1- < 5 years. Eight patients (29.6%) were in the age group 5 - < 10 years while seven patients (25.9%) were in the age group 10 -

16 years. This correlation was found to be statistically significant (p=0.00) as shown in {Table.10}.

T-10

3.8.2 Correlation between the grades of splenomegaly and its causes:

This correlation was found to be statistically significant (p=0.00). The two patients with massive splenomegaly (0.9%), one of them (50.0%) had haemolytic anaemia (Thalassemia) and the other one (50.0%) had Gaucher Disease. Huge splenomegaly was found to be present in 18 patients (08.3%); five of them (27.8%) were diagnosed as haemolytic anaemia. Visceral leishmaniasis was diagnosed in four patients (22.2%); Schistosomiasis was diagnosed in three patients (16.7%). Lymphomas were diagnosed in another three patients (16.7%), tropical splenomegaly in two patients (11.1%) and Myelofibrosis in only one patient (05.5%).

- Moderate splenomegaly was found in 69 patients (31.8%), 13 of them (18.8%) were due to leukaemia and 12 of them (17.4%) were in the undiagnosed group. Visceral leishmaniasis was found in nine patients (13.1%), haemolytic anaemia in seven patients (10.2%), schistosomasis in four patients (05.8%), Tropical splenomegaly in five patients (07.3%), malaria in three patients (04.4%)while tuberculosis in two patients (02.9%). Lymphomas were diagnosed in four patients (05.8%), cardiac diseases in two patients (02.9%), liver diseases in four patients (05.8%). Myelofibrosis was diagnosed

in one patient (01.4%), other infectious diseases in one patient (01.4%) and other diseases in another one patient (01.4%).

- Mild splenoemgaly was found in 88 patients(40.6%),25 of them(28.4%) had haemolytic anemia,13 of them (14.8%) had cardiac diseases and 12 patients (13.6%) had malaria. Undiagnosed splenomegaly was found in 10 of them (11.4%),other infectious diseases in nine patients (10.2%),iron deficiency anaemia in five patients (05.7%) ,schistosomiasis in four patients (04.6%), tuberculosis in four patients (04.6%) while other diseases was diagnosed in two patients (02.3%).This grade also occurred in only one patient (01.1%) in leukaemia, lymphoma, liver disease and tropical splenomegaly.

- Just palpable spleen was found in 40 patients (18.4%), 10 of them (25.0%) with haemolytic anaemias. It was also detected in eight patients (20.0%) with Malaria, seven patients (17.5%) with cardiac diseases and three patients (07.5%) with Tuberculosis. Other infectious diseases were diagnosed in five patients (12.5%); undiagnosed splenomegaly was also detected in five patients (12.5%), Iron deficiency anemia in one patient (02.5%) and leukaemia in one patient (02.5%) as shown in {Table 11].

3.9 Undiagnosed patients:

3.9.1 Age distribution:

- Twenty seven out of 217 patients in the study group were remained undiagnosed. Eight of these patients (29.7%) were in the age group 5-<10 years, seven patients (25.9%) were in the age group 10-16 years and six patients (22.2%) in the age group 1-< 5 years as well as in the age group less than 1 year as shown in [Fig. 22].

3.9.2 Grades of splenomegaly among the undiagnosed patients with splenomegaly:

- Among the 27 patients who were undiagnosed, 12 of them (44.5%) had moderate grade splenomegaly, 10 patients (37.0%) had mild grade splenomegaly while only five patients (18.5%) had just palpable spleens shown in [Fig.23].

3.10 THE OUTCOME:

During the study period and along with follow up of the 217 patients with splenomegaly who were admitted to the wards or who came in the referred clinics, we found that 82 patients (37.8%) were stable. Sixty-eight patients (31.3%) had recovered completely, 39 patients (18.0%) had improved, and 24 patients (11.1%) were lost for follow up while four patients (01.8%) had died. One of those patients died during splenectomy, one died because of hepatic failure while two patients died because of lymphoma as shown in [Fig. 24].

3.10.1 Correlation between grades of splenomegaly and the outcome:

Regarding the outcome of the patients in the study group in relation to the grades of splenomegaly, it was found to be statistically significant ($p = 0.018$). The only two patients with massive splenomegaly in the study group, one of them (50.0%) died while the other one (50.0%) was stable. The 18 patients with huge splenomeglay (08.3%), five of them (27.8%) were recovered completely while another five (27.8%) showed an improvement. Four patients (22.2%) were stable; three patients (16.7%) were lost for follow up while one patient (05.6%) died.

Moderate splenomegaly was found in 69 patients (31.8%), 20 of them (29.0%) recovered completely, 15 of them (21.7%) were improved, 24 of them (34.8%) were stable, eight of them (11.6%) were lost for follow up by their units while only two of them (02.9%) had died.

The 88 patients with mild grade splenomegaly (40.6%), 29 of them (33.0%) recovered completely while 36 of them (40.9%) were stable. Thirteen of them (14.8%) were lost for follow up while 10 patients (11.4%) were improved. The just palpable spleen was found among 40 patients (18.4%), 14 of them (35.0%) recovered completely, 17 patients (42.5%) were stable while nine patients (22.5%) had improved.

3.11 Treatment of the patients with splenomegaly in the study group:

Most of the patients, 215 patients (99.1%), received medical treatment according to the cause of splenomegaly while only two patients (0.9%) underwent surgical treatment.

3.11.1 Correlation between the grades of splenomegaly and the treatment in the study group:

Among the 215 patients who were treated medically (99.1%), 88 of them (40.9%) had a mild grade splenomegaly while 69 of them (32.1%) had a moderate grade splenomegaly. Forty patients (18.6%) had just palpable spleen, 17 patients (07.9%) had a huge splenomegaly while only one

patient (0.5%) had a massive splenomegaly. The only two patients who had undergone surgical treatment, one of them (50.0%) had a huge splenomegaly and the other one had a massive splenomegaly. This relation was found to be statistically significant (p = 0.000) as shown in {Fig.25}.

3.11.2 Correlation between treatment and the outcome in the study group:

In the 215 patients who were treated medically (99.1%), 67 of them (31.2%) had recovered completely while 82 patients (38.1%) were stable after the medical treatment. Thirty nine patients (18.1%) had improved, 24 patients (11.2%) were lost for follow up while three patients (01.4%) died. Regarding the two patients who had undergone surgical removal of their huge spleen, one of them (50.0%) was stable and the other one (50.0%) with Gaucher Disease died during the operation as shown in [Fig. 26].

Chapter Four

4. DISCUSSION

4.1. DEMOGRAPHIC CHARACTERISTICS:

Th`e ages of children in this study ranged from 0-16 years, with the peak age group of 0-5 years (42.0%). This goes in line with what was mentioned in a previous study done in the Ivory Coast [82].

The study showed an obvious male predominance (62.2%). This can be explained by the appearance of more cases of splenomegaly among patients with haemolytic anaemias; which are X- linked in some of them such as G6PD. This finding was documented in many studies done in Ivory Coast and Duke [74, 82].

The majority of children in this study belong to Arab tribes, Baggara and Kordufanian and Darfurian tribes representing a percentage of (41.5%), (16.1%) and (21.7%) respectively. However, there is a study that was carried out in Gambia, which studied the ethnic differences in the prevalence of splenomegaly and malaria. Significant variations among members of three main ethnic groups who were resident there were found [80]. In our study, the clustering of splenomegaly among certain tribes could be explained by the increased prevalence of splenomegaly in diseases that may have a genetic predisposition like Haemolytic anaemias. Residence of

children in an endemic area with certain disease may be attributed to this variation.

4.2 FAMILY AND SOCIAL HISTORY:

Consanguinity was observed among the majority of parents, constituting (68.2%), while far relationship was noticed in (18.0%) and no consanguinity in (13.8%). However, there was no previous study that can support this observation. Although this consanguineous marriage is a common practice in our community, yet it could be a risk factor for transmission of an inherited disease that leads to splenomegaly.

The majority of fathers were illiterate (68.2%), while (66.3%) of mothers were illiterate too. This has an impact on decreasing their knowledge and delaying their seeking of medical advice regarding splenomegaly and associated diseases in their children. However, data supporting this is lacking.

The majority of fathers were unskilled labrourers (60.4%), while the majority of mothers (44.0%) were housewives. This may be well reflected by the family income, which may lead to a delay in diagnosing the cases with splenomegaly because of the enormous cost of many investigations, which the family could not afford.

The majority of children (79.3%) belong to families of low social class and the rest (20.7%) belong to a moderate social class. No cases belong to high social class. This could be a true reflection of the social back ground in Sudan.

4.3. School attendance:

Twenty-five patients (11.5%) had an irregular school attendance, four patients (01.8%) repeated the year because of poor performance and fifty-six patients (25.8%) were off school. This could be explained by their chronic illnesses that necessitated repeated hospital visits. However, data supporting this affection of splenomegaly in school attendance are lacking.

4.4. Symptoms:

The most common reason of presentation in the study group was found to be fever, constituting (96.3%), followed by abdominal pain (55.8%), abdominal distension (47.9%), general ill health (47.9%), bone pain (32.7%) and weight loss (31.8%). These findings are consistent with what was found in previous studies done in Paris and Brazil [75, 82], except for jaundice, which is less represented in our study. This could be explained by the lack of good observation of mild jaundice that is associated with haemolytic anaemias which was found to be the commonest cause of splenomegaly in our study. Cough and shortness of breath were reported in

(28.1%) and this is related to the cardiac causes of splenomegaly. Lower limb swelling, Diarrhoea, haematuria and convulsions were less reported in this study.

4.5. SIGNS:

Hepatomegaly was the commonest finding on examination of the patients with splenomegaly, constituting (91.2%). This is may be due to the etiologies of splenomegaly, which may lead to hepatomegaly as well. This is goes with the finding of previous studies done in evaluation of patients with hepatosplenomegaly [75]. Pallor was observed in (83.9%) and this is also because of the predominance of anaemias and infectious diseases as causes of splenomegaly. This goes in line with studies done in Brazil, India and Gambia[75,80,87].

Abdominal distension was found in (75.6%) of the children and this is related mainly to hepatosplenomegaly rather than ascites, which was reported in (05.1%) only. This is consistent with what was found in Zambia, Paris and India [81, 82, 87]. Lymphadenopathy was found in (20.7%) and this goes with the prevalence of causes of splenomegaly that may lead to lymphadenopathy like leukemia (06.9%), lymphoma (03.7%), visceral leishmaniasis (06.0%) and some of other infectious diseases (06.9%). Jaundice was observed in (23.5%) and this is consistent with the prevalence of haemolytic anaemias in our study group and also consistent

to more or less with previous study that was done in Brazil, which showed a prevalence of (16.0%) of this diseases[75]. Clubbing of fingers was not common (02.8%) because the commonest causes of splenomegaly in our study group were not known to cause this sign. However, data supporting this finding are lacking.

Heart murmurs were reported in (18.4%). More than half of them were due to cardiac diseases and the rest were considered as haemic murmurs associated with severe anaemia in some cases. Other signs like petechial or purpuric rash (04.1%), eczema (0.5%), visible dilated abdominal veins (05.1%), abdominal tenderness (07.4%), lower limb oedema (06.0%) and joint deformity (01.8%) were less reported in our study group. These findings are similar, to more or less extent, with which were written in the literature[75,77,81].

4.5.1. Grades of splenomegaly:

The grading of splenomegaly into five grades according to the enlargement in relation to specific anatomical point was adopted in this study. It's more accurate than measuring the enlargement of spleen by centimeters, which may differ from person to person. The commonest grade among the study group was found to be the mild one constituting (40.6%). This is followed by the moderate grade (31.8%), just palpable spleen in (18.4%), Huge splenomegaly (08.3%) while massive

splenomegaly was the least grade encountered (0.9%). This can be explained by the prevalence of diseases that lead to mild or moderate enlargement of spleen among Sudanese children more than the diseases that lead to huge or massive splenomegaly. However, there was no data that can support this result from previous studies regarding splenomegaly and the associated diseases.

4.6. INVESTIGATIONS:

General investigations were done in all patients in the study group (217 patients), who had splenomegaly regardless of the clinical presentation. These included Hb, WBC, platelets count and peripheral blood picture (CBC), blood film for malaria, urine general and stool general. According to the clinical evaluation and the results of the general investigations a second line or specific investigations were done. These included sickling test, (LF.T), abdominal ultrasound, bone marrow aspiration or trephine biopsy and lymphnode biopsy. Many sets of investigations required for confirmation of many causes of splenomegaly were lacking in our hospitals and some of them are not available in Sudan. These including IgM level, Histopathology for splenic or liver biopsies, metabolic screening in blood and urine and some of advanced imaging techniques. This has affected the final outcome of proper diagnosis and lead to many undiagnosed cases and consequently mismanagement in a lot of patients. A previous study in

Pakistan concluded that haematological workup is informative in most of cases with splenomegaly and bone marrow examination is the key investigation [85].

4.7. Causes of splenomegaly in the study group:

Haemolytic anaemias were found to cause splenomegaly in 48 patients (22.1%). This diagnosis included conditions such as Sickle Cell Disease, Thalassemia, (G6PD) and Auto immune Haemolytic Anaemia. Sickle Cell Anaemia was found to be the commonest anaemia among the children with haemolytic anaemia constituting (79.1%) of them. This is similar to what was found in Brazil [75]. Malaria was found in 23 patients (10.6%) only and this is unlike what was reported by Timite and his colleagues in their study about etiology of splenomegaly in children in the tropics, where Malaria came at the top of their lists of causes [80,82]. This can be explained by that all cases of malaria in our study who required admission to hospital were cases of severe Malaria. Most cases of Malaria were treated as an outpatient unless it became complicated and necessitated admission to Hospital.

Schistosomiasis was found in 11 patients (05.1%). This is unlike what was reported in a study that was carried out in Kenya. Schistosomiasis in that study was one of the commonest causes of splenomegaly in children in Africa [91]. Visceral Leishmaniasis was diagnosed in 13 patients (06.0%), in

nine of them (69.2%) the diagnosis was based on the presence of amastigote in bone marrow aspiration. Four patients were considered to have the disease depending on the clinical findings and suspicion. This incidence was similar to what was reported in Brazil [75], but it was less than the reported cases in Turkey [92] where forty children with fever and splenomegaly found to be due to Visceral Leishmaniasis. Splenic aspiration, with some precaution is a safe and easy method for the diagnosis. This is proved by what was reported by Thakur CP and his colleagues in a study that was carried out in India and Kenya[93,94]. This procedure gave a positive result more often than bone marrow aspiration. In our hospitals we depended on bone marrow aspiration or lymph node aspiration more than splenic aspiration. Direct Agglutination Test (DAT) was the most available test in our hospital. This test was found to be a useful screening test with a sensitivity of 94% and a predictive value of negative test of 92%. Elhassen AM and his colleagues in a study done in Sudan 1991 proved this [95]. Tuberculosis was diagnosed in nine patients (04.1%). This is more or less the same as what was reported in Brazil and Paris[75,82].

Malignancies were diagnosed in 23 children (10.6%) included leukaemias in 15 patients (06.9%) and lymphomas in 8 patients (03.7%). This is similar what was reported in Brazil and USA[75,77]. Timite in his study

reported leukaemia and lymphoma as relatively infrequent causes of splenomegaly[82].

Tropical splenomegaly was suspected to be the cause of splenomegaly in eight patients (03.7%). This had been suggested after exclusion of other causes although no specific investigations like IgM level or liver biopsy for sinusoidal infiltration with lymphocytes has been done to these patients. However, the diagnosis was suspected and accordingly antimalarial treatment was prescribed. During follow up marked regression of the size of spleen was noticed. This had supported this diagnosis inspite of lack of investigation that might have confirmed it. This incidence is not acceptable to that reported in the literature [82]. In Ghana 41 patients out of 221 with massive splenomegaly was found to have tropical splenomegaly[96].

Iron deficiency anaemia was found in seven patients (03.2%) who improved after Iron supplementation. In the literature this cause of splenomegaly was included with other types of anaemia, or found to be a concomitant cause associated with other disease like Idiopathic Thrombocytopenic Purpura in Arab children.[96].

Other infections like Typhoid fever, Brucellosis, HIV, Infectious Mononucleosis were reported in 15 patients (06.9%). This is not consistent with what was reported by Timite in his study (82), where salmonella

infection alone represented (15%) of the cases and HIV represented (03%). Also it is unlike what was reported in Yemen by H.A. Shamahy et al, where the frequency of splenomegaly among patients affected by Brucella infection was (78.7%) out of the 47 patients[97]. Other diseases like Myelofibrosis, storage disease like Gaucher disease, chronic Idiopathic thrombocytopenic purpura and (SLE) were less frequent. However, this is goes in line with what was reported in the literature[75,82].

In our study, 27 patients (12.4%) were not diagnosed by the available investigations in the hospitals where they were admitted. This group of patients required more investigations that were not available at our set-up like serological tests, facilities for splenic and liver biopsies and proper histopathology. However, this incidence is similar to what was reported about undiagnosed patients with splenomegaly in Ghana [96].

4.8. Treatment of patients with splenomegaly in the study group:

Most of the patients (99.1%) in the study group received medical treatment according to the cause of splenomegaly. Only two patients (0.9%) undergone splenectomy because of massive splenomegaly that was complicated by hypersplenism. However, splenectomy in our hospitals was not a common procedure because of fear of sepsis and infections by encapsulated bacteria. The lack of vaccines which was recommended for patients who were splenectomized or had functional asplenia like sickler

patients, was also an attributable cause. Laparoscopic splenectomy must be encouraged because it is feasible and safe, especially in children with hematologic disorders[98].

4.9. The Outcome in the study group:

During the study period 82 patients (37.8%) were stable, 68 patients (31.3%) had recovered completely from their illnesses that caused the splenomegaly. Thirty nine patients (18.0%) were improved and the spleen regressed in size, 24 patients (11.2%) were lost for follow up while only four patients (01.8%) were died because of severity of their illness, one of them with Gaucher disease died intraoperatively. Because most of the patients reside far away from the hospital and the short duration of study period this result may not be perfect enough to reflect the actual outcome of these patients.

In this study (12.4%) of the study group remained undiagnosed as the causes of their splenomegaly were undetermined. This is comparable to what was published world- wide. All Hospitals were lack some of the important investigations that may help in the diagnosis of such cases. This is aggravated by the lack of federal support to these Hospitals. However, this may increase the financial and psychosocial burden upon the patients and the family. Improvements in investigations and management of such cases have to be considered. Furthermore, children who had splenectomy

remain at risk of immunodeficiency. They require lifelong vaccines which are not commonly available and not easily accessible. Moreover, their cost is enormous leading to further financial burden on the families.

CONCLUSIONS AND RECOMMENDATIONS

5.1. CONCLUSION:

- Splenomegaly was more common among the age group 10 -16 years and it was characterized by male predominance.
- Tribal origin, consanguineous marriage and social status seem to affect the causes and the clinical presentation of children with splenomegaly.
- Fever was the commonest clinical presentation followed by abdominal pain, abdominal distension, general ill health, and bone pain and weight loss.
- The main signs in the study group were hepatomegaly, pallor, abdominal distension, dyspnoea, jaundice, lymphadenopathy, ascites and visible dilated abdominal veins.
- Mild splenomegaly was the commonest grade, followed by moderate grade, just palpable spleen, huge splenomegaly and lastly massive splenomegaly.
- The common causes of splenomegaly in the study group were haemolytic anaemias mainly Sickle Cell Disease; Followed by Malaria,

cardiac diseases, Schistosomiasis, Visceral Lieshmaniasis, Tuberculosis, Tropical splenomegaly and other infectious diseases. There was high percentage of undiagnosed patients.

- Investigations which were available in most Hospitals in the study area including haematological investigations, abdominal Ultrasound and bone marrow aspiration. Specific investigations such as serum IgM level, Biopsies for liver and spleen and certain imaging studies were not available.

- The majority of patients received medical treatment while only two patients undergone surgical treatment (splenectomy).

- By the end of the study (37.8%) of the patients were stable, (31.3%) had recovered completely from their illnesses and the spleen regressed in size. Furthermore, (18.0%) had improved but still had splenomegaly, (11.1%) were lost for follow up while (01.8%) had died.

5.2 RECOMMENDATIONS:

- The awareness of the parents that splenomegaly can occur as a consequence of various causes, with variation in the presenting complaints, should be increased through sessions of health education at the referred clinic and ward.
- The awareness of all treating doctors should be raised about the importance of proper clinical evaluation and proper haematological work up for any patient with palpable spleen to rule out serious causes.
- All hospitals need a proper setup of investigations that can confirm the causes of splenomegaly such as serum IgM level. Histopathology for liver and splenic biopsies must be included as part of investigating children with unexplained splenomegaly.
- Certain protocol for investigating and management of children with splenomegaly must be provided to all paediatrics hospitals. This protocol must include clear indications for splenectomy and advices regarding activities and sports that the children need to avoid or modify.

- Vaccine, H.Infleunzae and pneumococcal, should be made available, accessible and affordable for those children who have auto or surgical splenectomy.
- Further studies and researches should be carried out regarding different aspects of splenomegaly.

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